MCP-274

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Joseph Luber

Serial No.: 09/966,493 Art Unit: 1615

Filed : September 28, 2001 Examiner: R. M. JOYNES

For : IMMEDIATE RELEASE TABLET

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November 12, 2003
(Date of Deposit)

Sharon E. Hayner
Name of applicant, assignee, or Registered Representative

(Signature)

November 12, 2003
(Date of Signature)

Assistant Commissioner for Patents
Washington, D.C. 20231

APPEAL BRIEF

Real Party in Interest

The real party in interest is McNeil-PPC, Inc., the assignee of the application.

Related Appeals and Interferences

None.

Status of the Claims

Claims 1-20 are original to the application and have been finally rejected in the Office Action mailed June 12, 2003. Claims 1-20 are on appeal herein.

Status of Amendments

No amendments to the claims have been filed subsequent to the final rejection. However, a Response and Declaration under 37 C.F.R. §1.132 mailed September 12, 2003 have been entered by the Examiner.

Enclosed is the original Declaration under Section 132 bearing Joseph Luber's signature.

Summary of the Invention

In a first embodiment (claim 1), the present invention relates to an immediate release tablet comprising at least 60 weight % of an active ingredient and a powdered wax having an melting point greater than about 90° C, said tablet meeting the USP dissolution specifications for immediate release tablets containing said active ingredient.

In a second embodiment (claim 17), the present invention relates to an immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax, paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is prepared by direct compression.

In a third embodiment (claim 18), the present invention relates to an immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax, paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is substantially free of water-soluble, non-saccharide polymeric binders.

In a fourth embodiment (claim 19), the present invention relates to an immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax, paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is substantially free of hydrated polymers.

Issues

1. Whether claims 1-6, 9, 10 and 16-20 are obvious under Section 103 over US Patent No. 5,494,681 to Cuca et al.

2. Whether claims 7 and 8 are obvious under Section 103 over Cuca in view of US Patent No. 5,098,715 to McCabe et al.

3. Whether claims 11-15 are obvious under Section 103 over Cuca in view of US Patent No. 5,681,583 to Conte et al.

Grouping of Claims

The claims are grouped separately for purposes of this appeal as follows: 1) claims 1-16; 2) claims 17 and 20; 3) claim 18; and 4) claim 19. (See separate embodiments under "Summary of the Invention".)

Argument

Claims 1-6, 9, 10, and 16-20 have been rejected as obvious over Cuca et al. The Examiner argues Cuca teaches a pharmaceutical delivery system comprising an active ingredient, a wax material and a hydrophobic material. The Examiner states that the active ingredient can be selected from one of several categories, and be present in an amount ranging from about 5% to about 65%. The Examiner also argues that the types and amounts of wax materials overlap with the claimed invention.

Claims 7 and 8, which recite the tablet of claim 1 having an outer coating, have been rejected as obvious over Cuca in view of McCabe et al. McCabe is cited to show the use of outer coatings in a dosage form.

Finally, claims 11-15, which recite the tablet of claim 1 containing an insert that may contain active ingredient, have been rejected as obvious over Cuca in view of Conte et al. Conte is cited to show the use of two active ingredients within the same dosage form.

Applicants maintain that the rejections of record are without merit. There is a fundamental difference between the primary reference, Cuca, and the claimed invention. Cuca teaches the use of melted wax, while the claimed invention employs powdered wax.

Specifically, Cuca discloses a pharmaceutical delivery system comprising a) an active material, and b) a spatially oriented matrix. The spatially oriented matrix in turn comprises (i) a wax core material, and (ii) a regional hydrophobic polymer. Cuca's dosage form is made by melting the wax and the hydrophobic polymer together into a liquid, and then adding the active ingredient thereto. A slurry or dispersion is thereby formed and then cooled. See column 5, line 64 to column 6, line 46. See also all of Cuca's examples.

On the other hand, each of the independent claims herein recite that the wax is "powdered." It should be noted that this is not a mere process step, as suggested by the Examiner. The physical state of the wax is an element of the claimed invention.

The use of powdered wax according to the invention results in tablets having substantially better dissolution than tablets in which the wax has been melted. As set forth in the Declaration, Mr. Luber made four batches of tablets each containing acetaminophen (APAP) and other excipients. In addition, each batch of tablets contained one of four waxes. The formulations were identical except for the wax used. For each batch, one portion of the tablets were heated to melt the wax, and one portion were not. All of the tablets were then tested for APAP dissolution according to the procedure of USP 26 under the Acetaminophen Tablet monograph.

The tablets in which the wax had been melted (comparative) demonstrated markedly inferior APAP dissolution results compared to the tablets containing powered wax according to the invention. The highest amount of APAP dissolved among the melted tablets was achieved by the carnauba wax batch, which at best dissolved only 79% of the APAP in 30 minutes. In contrast, the tablets according to the invention, regardless of the wax employed, dissolved at least 94% of the APAP in 15 minutes. These results are consistent with the fact that applicants' tablets are immediate release dosage forms. Each of independent claims 1, 17, 18, and 19 recites "[a]n immediate release tablet." In addition, claim 1 also recites, "said tablet meeting the USP dissolution specifications for immediate release tablets containing said active ingredient." Accordingly, the comparative tablets in which the wax had been melted neither contained powdered wax nor met the immediate release properties for APAP dissolution.

In spite of applicants' data, the Examiner argues that the Declaration is not commensurate in scope with the claims. In the Advisory Action mailed October 2, 2003, the Examiner questioned whether one could accurately judge the results given that four different waxes were used and the melting points of the waxes were not specified. The Examiner also questioned whether the dissolution testing at 15 and 30 minutes was relevant to an immediate release formulation.

As for the use of different waxes, the comparison to be made here is between the melted and unmelted versions using the same wax, not between different batches using different waxes. Whether different waxes behave differently from each other is not relevant here. The data clearly shows that two tablets containing the same ingredients, including the same wax, have substantially different dissolution properties depending on whether the wax has been melted or not. This is true regardless of which wax is used.

On the issue of immediate release dissolution testing, it should be noted that testing was performed according to USP 26 under the Acetaminophen Tablet monograph, which is certainly familiar to one skilled in the art of tablet formulation. A copy of USP 26 is attached. To meet the standards of USP 26, not less than 80% of the APAP must dissolve within 30 minutes. See page 2, line 3, of the attached entitled "Tolerances." As an extra step, Mr. Luber also measured dissolution at 15 minutes, although this is not required by the USP method. Dissolution was performed at 37° C. In sum, the dissolution data was generated according to the appropriate USP method for immediate release APAP tablets.

It should be noted that neither McCabe nor Conte remedies the deficiencies of Cuca. It should also be noted that none of the cited references teach or suggest other embodiments of the invention. For example, claims 17 and 20 recite an immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax, paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is prepared by direct compression. Cuca is made by a slurry process, as described above, which is not the same as or similar to direct compression. Nor do McCabe or Conte teach or suggest a tablet made by direct compression from a combination of active ingredient and wax.

Claim 18 recites an immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax, paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is substantially free of water-soluble, non-saccharide polymeric binders. A teaching or suggestion of substantially eliminating water-soluble, non-saccharide polymeric binders from an immediate release tablet containing a combination of active ingredient and wax is not found in Cuca, McCabe, or Conte either.

Finally, claim 19 recites an immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax, paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is substantially free of hydrated polymers. None of Cuca, McCabe, or Conte, alone or in combination, teaches or suggests substantially eliminating hydrated polymers from an immediate release tablet containing a combination of active ingredient and wax.

Conclusion

For these reasons, applicants maintain the claims are patentable. Applicants' Declaration is indeed commensurate in scope with the claimed invention. Reversal of the rejections of record is respectfully requested.

Please charge Deposit Account No. 10-0750/MCP-274/SEH in the name of Johnson & Johnson all fees required in connection with this paper. This Authorization is being submitted in triplicate.

Respectfully submitted,

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APPENDIX
CLAIMS ON APPEAL

1. An immediate release tablet comprising at least 60 weight % of an active ingredient and a powdered wax having an melting point greater than about 90° C, said tablet meeting the USP dissolution specifications for immediate release tablets containing said active ingredient.

2. The tablet of claim 1, wherein the active ingredient is selected from the group consisting of acetaminophen, ibuprofen, calcium carbonate, magnesium hydroxide, magnesium carbonate, magnesium oxide, aluminum hydroxide, mixtures thereof, and pharmaceutically acceptable salts thereof.

3. The tablet of claim 1, wherein the wax is selected from the group consisting of linear hydrocarbons, microcrystalline wax, and mixtures thereof.

4. The tablet of claim 1 prepared by direct compression.

5. The tablet of claim 1 which is substantially free of water-soluble, non-saccharide polymeric binders.

6. The tablet of claim 1, which is substantially free of hydrated polymers.

7. The tablet of claim 1 further comprising at least one outer coating.

8. The tablet of claim 7, wherein the outer coating comprises a material selected from the group consisting of gelatin, isomalt, monosaccharides, disaccharides, polysaccharides such as starch, cellulose derivatives, shellacs, polyhedric alcohols such as xylitol, mannitol, sorbitol, maltitol, erythritol, and polyalkylene glycols.

9. The tablet of claim 1 comprising up to about 20 weight percent wax.

10. The tablet of claim 1 further comprising an excipient selected from the group consisting of disintegrants, flow aids, and optionally lubricants.

11. The tablet of claim 1 further comprising an insert disposed within tablet.

12. The tablet of claim 11, wherein the insert comprises additional active ingredient.

13. The tablet of claim 12, wherein the additional active ingredient has a different release profile from the active ingredient in the tablet.

14. The tablet of claim 12, wherein the amount of additional active ingredient is from about 0.1 to about 30 mg.

15. The tablet of claim 12, wherein the additional active ingredient is selected from the group consisting of loratadine, fexofenadine, cetirizine, chlorpheniramine, brompheniramine, diphenhydramine, pseudoephedrine, cyproheptadine, montelukast, loperamide, famotidine, dexamethasone, hydrocortisone, cyclobenzaprine, alendronate, hydrochlorthiazide, rofecoxib, indomethacin, ketoprofen, meloxicam, piroxicam, lovastatin, atorvastatin, pravastatin, simvastatin, finasteride, and pharmaceutically acceptable salts, esters, and mixtures thereof.

16. The tablet of claim 1, wherein the particle size of the wax is in the range of about 5 to about 100 microns.

17. An immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax,

paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is prepared by direct compression.

18. An immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax, paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is substantially free of water-soluble, non-saccharide polymeric binders.

19. An immediate release tablet comprising at least 60 weight percent of an active ingredient and a powdered wax selected from the group consisting of shellac wax, paraffin-type waxes, polyethylene glycol, and mixtures thereof; wherein said tablet is substantially free of hydrated polymers.

20. The tablet of claim 17, wherein said active ingredient is in its native crystalline form.

Acetaminophen Tablets

» Acetaminophen Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_8H_9NO_2$.

Packaging and storage— Preserve in tight containers.

Labeling— Label Tablets that must be chewed to indicate that they are to be chewed before swallowing.

USP Reference standards ⟨ 11 ⟩— *USP Acetaminophen RS*.

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation* obtained as directed in the *Assay*.

B: Triturate an amount of powdered Tablets, equivalent to about 50 mg of acetaminophen, with 50 mL of methanol, and filter: the clear filtrate (test solution) responds to the *Thin-layer Chromatographic Identification Test* ⟨ 201 ⟩, a solvent system consisting of a mixture of methylene chloride and methanol (4:1) being used.

Dissolution ⟨ 711 ⟩—

Medium: pH 5.8 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*); 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure— Determine the amount of $C_8H_9NO_2$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 243 nm on filtered portions of the solution under test.

suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of *USP Acetaminophen RS* in the same *Medium*.

Tolerances— Not less than 80% (*Q*) of the labeled amount of $C_8H_9NO_2$ is dissolved in 30 minutes.

F OR TABLETS LABELED AS CHEWABLE—

Medium: pH 5.8 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*); 900 mL.

Apparatus 2: 75 rpm.

Time: 45 minutes.

Procedure— Proceed as directed for *Procedure* for *Acetaminophen Tablets*.

Tolerances— Not less than 75% (*Q*) of the labeled amount of $C_8H_9NO_2$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨ 905 ⟩: meet the requirements.

Assay—

Mobile phase, Standard preparation, and *Chromatographic system*— Proceed as directed in the *Assay* under *Acetaminophen Capsules*.

Assay preparation— Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of acetaminophen, to a 200-mL volumetric flask, add about 100 mL of *Mobile phase*, shake by mechanical means for 10 minutes, sonicate for about 5 minutes, dilute with *Mobile phase* to volume, and mix. Transfer 5.0 mL of this solution to a 250-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Filter a portion of this solution through a 0.5-µm or finer porosity filter, discarding the first 10 mL of the filtrate. Use the clear filtrate as the *Assay preparation*.